REMARKS

Claim 16 has been amended to include the term "acid" following the term "nucleic." Claims 20 and 29 have been amended to include the phrase "wherein the chromosome fragment contains the exogenous nucleic acid." These amendments simply introduce language that is already set forth in claims 1 and 19, from which claims 20 and 29 depend. Thus, these amendments do not narrow the scope of claims 20 and 29. The Examiner's suggestions have been appreciated.

The Examiner has indicated that the information disclosure statement filed July 3, 2003 fails to comply with 37 CFR § 1.98 (a)(3) because it does not include a concise explanation of relevance. Applicants hereby include an English-translation summary of the *de Kochko* reference. It is believed that the English-translation summary is a concise explanation of relevance of the *de Kochko* reference to the current application.

35 U.S.C. § 112 - INDEFINITENESS

Claims 1-16, 19-29, and 36-42 have been rejected as indefinite on the ground that the preambles of claims 1, 19, and 38, directed to methods for making a plant artificial chromosome, are inconsistent with the last method steps recited therein, which recite that the chromosomes are contained in fused protoplasts or cells derived therefrom. The Examiner's suggestions for amending the claims have been appreciated, but Applicants respectfully submit that the claims are clear and definite as they presently stand. The fact remains that the claims do require the formation or "making" of an artificial chromosome. The claims are not rendered indefinite simply because the immediately external environment is a fused protoplast or cell. Applicants respectfully request withdrawal of the rejection.

The Examiner has rejected claim 2 as being indefinite on the ground that the recitation "irradiated" is unclear in terms

of the specific means with which the irradiation is accomplished. Applicants respectfully disagree. The term "irradiation" would be readily understood by persons skilled in the art, particularly as read in light of the specification. Irradiation techniques are disclosed in the specification (*e.g.*, p. 7, lns. 15-16, and example 2, p. 16, line 17-18, teaching that "protoplasts were irradiated with gamma rays (100 krad) from a cobalt60 source"). Reconsideration and withdrawal of the rejection are respectfully requested.

In response to the rejection of claim 10, Applicants submit that as disclosed on page 6, lns. 15-16, stable transformed cell lines (and the protoplasts derivable therefrom) may be obtained from a whole plant regenerated following transformation and selection. Applicants respectfully request the withdrawal of this rejection.

The Examiner has rejected claim 11 as indefinite on the ground that it must yield the protoplasts that are used in step (b) of claim 1. Applicants disagree. Claim 11 recites regenerating a whole plant from the fused protoplasts of step 1(**d**). Applicants respectfully request the withdrawal of this rejection.

Claim 12 has been rejected as indefinite on the ground that the recitation "recombination site" is unclear and how it differs from a "restriction site". Applicant submits that persons skilled in the art would readily understand these terms, particularly as read in light of the specification. See, *e.g.*, the disclosure on pages 10-11. Applicants respectfully request withdrawal of this rejection.

The rejection of claims 20 and 29 has been addressed by amending the claims as per the Examiner's suggestion.

35 U.S.C. § 112 - WRITTEN DESCRIPTION

Claims 20-35 and 42 are rejected as failing to comply with the written description requirement. The Examiner has alleged

that the specification does not adequately describe the genus of recombinant nucleic acids, vectors, or recombinant cells comprising them; isolated plant cells, protoplasts, whole plants or seeds derived from them, or hybrid plant cells or species encompassed by the claims. The Examiner has also alleged that not all members of the claimed genus of nucleic acids, protoplasts, plant cells and plants, etc., will have the same structure and function. Applicant respectfully traverses the rejection.

The claimed products have in common a chromosome fragment or in the case of recombinant nucleic acid of claims 30-35, that exhibits normal plant chromosomal activities. Regardless, these aspects of the present invention are disclosed in the specification in a manner that complies with the statute. Granted, not every embodiment embraced by the claims is exemplified in the specification. Then again, the law does not require such exemplification, even in an unpredictable art. Contrary to the allegation set forth on page 6 (supported by the *Fiers* decision), Applicant is not relying on the disclosure of the method to provide the requisite (written description) support for the claimed products. The specification, e.g., working examples 1-3, provides the necessary support to satisfy written description. Reconsideration and withdrawal of the rejection are respectfully requested.

35 U.S.C. § 112 - ENABLEMENT

The Examiner has rejected claims 1-16 and 18-42, as lacking enablement on two separate grounds. First, the Examiner has alleged that the specification does not enable fragmentation of chromosomes by any means other than gamma-radiation (Office Action p. 9), and that such direction is lacking in the prior art. Applicants disagree; *prima facie* lack of enablement has simply not been established.

The disclosure on page 7, lns. 12-22 provides teachings directed to fragmentation of chromosomes. Irradiation and treatment with chemical agents are explicitly disclosed. Four (4) prior art publications are referenced. Despite the statement that "direction is lacking in the prior art," the Office action contains no explanation as to why these 4 publications are deficient such that when considered together with the teachings in the specification, would not enable a person skilled in the art to produce fragmented chromosomes in plants. The Examiner is reminded again that applicants do not have to disclose each and every embodiment embraced by their claims, let alone exemplify them, even in an unpredictable art. Aside from the foregoing, other irradiation techniques are well known in the art, including UV-treatement (Hall *et al.*, 1992, *Mol. Gen. Genet.*, 234, 315-324), and heavy ion treatment (Tobias, CA. 1985, *Radiation Res.*, 103, 1-33). Accordingly, persons skilled in the art would have been enabled to practice the claimed invention without resorting to undue experimentation to determine how to produce chromosome fragments using methods other than gamma irradiation. Reconsideration and withdrawal of this ground of rejection are requested.

Second, the Examiner has alleged that because the specification teaches that irradiation makes the host "non-viable," it would not be possible to cross the irradiated plant with another plant in order to effect a transfer of nucleic acid and create the artificial chromosomes (Office Action p. 10). This proposition is incorrect. As disclosed on page 7, lns. 23-28 of the specification, the ensuing protoplast fusion or crossing effectively revitalizes or revives the protoplast/plant containing the fragmented chromosomes (*e.g.*, "The purpose of fusing the treated protoplasts with non-transformed protoplasts is to revive the transformed protoplasts from the effects of the chromosomal disruption e.g., caused by irradiation or chemical

treatment."). Reconsideration and withdrawal of this ground of rejection are requested.

The Examiner has also rejected claims 30-35 and 42 for lack of enablement. It appears that this rejection is based on an allegation that non-recited constituents of chromosomes that may affect the functions of the nucleic acids are not enabled. The Examiner has also alleged that claim 33 is not enabled for all cell types, particularly given that the claimed nucleic acids "are not functional in non-plant and non-yeast cells." Applicants respectfully traverse the rejection.

In response, Applicant submits that the claims are enabled. Specifically, it teaches which chromosomal elements are important in order for a chromosome fragment to exhibit normal plant chromosomal activities. See, e.g., pages 5-6. Claim 33 is enabled too. Contrary to the allegation in the Office action, the claimed nucleic acids are recited in terms of cell types in which they are functional, as opposed to cell types in which they are nonfunctional. Accordingly, Applicant respectfully requests the withdrawal of this ground of rejection.

35 U.S.C. § 103 - OBVIOUSNESS

The Examiner has rejected claims 1, 2, 5-16 and 18-42 as being obvious in light of three references, namely Famelaer, *et al.*, Blume, *et al.*, and Adam, *et al.* The Examiner has alleged that *Famelaer* teaches the production of plants produced by fusing protoplasts with non-treated protoplasts and *Blume* teaches the insertion of a coding region into a restriction enzyme site in a plant transformation vector prior to introduction into the plant. Thus, the Examiner has concluded that it would have been obvious to one of ordinary skill in the art to modify the teachings of *Famelaer* by producing protoplasts from transgenic plants as taught by Blume. Moreover, the Examiner believes it would have also been obvious to use YAC

vectors, as taught in *Adam*, to transform a plant prior to protoplast isolation, irradiation, and fusion with non-treated protoplasts. Applicants respectfully traverse the rejection.

Famelaer teaches the production of parasexual hybrid plants produced through fusion of irradiated protoplasts with non-irradiated protoplasts (p. 518-519). It simply shows that plants made sterile through gamma-irradiation can be back-crossed with fertile plants to exhibit selected sexually transmitted chromosome traits (p. 513). *Famelaer* does not teach or suggest the transformation of the protoplasts with exogenous nucleic acid before chromosome fragmentation, or selecting or identifying fused protoplasts or cells derived from the fused protoplasts that contain chromosome fragments containing the exogenous nucleic acid, and that exhibit normal plant chromosomal activities, as claimed in the present application. Moreover, *Famelaer* had problems with unstable transmission rates with first and second-generation progeny and saw a decrease in transmission rates when the first-generation plants were fertile (p. 516). Thus, *Famelaer* also teaches that multiple generational crossings are needed to overcome both infertility and unstable transmission rates.

The teachings of the secondary references, when considered collectively along with *Famelaer*, would not have supplied its deficiencies from the standpoint of the claimed invention. They simply teach known plant transformation methodologies. *Blume* teaches insertion of the GUS coding region into restriction enzyme sites in a plant transformation vector before introducing it into a plant. As shown in the discussion section, *Blume* merely investigates the transcriptional regulation of ACC oxidase gene expression by using GUS to monitor a region of nucleotides (p. 741-742). *Adam* teaches the use of YAC vectors to stably transform plant cells.

Thus, neither *Blume* nor *Adam* teaches nor suggests modifying the methods or genetic constructs of *Famelaer* such that one of ordinary skill in the art would have been motivated to produce the claimed invention with a reasonable expectation of success. In short, the prior art, whether viewed individually or collectively, does not suggest introducing exogenous nucleic acid into a recipient plant or part thereof such that it is contained in a chromosome fragment that exhibits normal plant chromosomal activities, indirectly via a donor that had been treated so as to produce chromosome fragments, prior to transfer. Thus, the cited references could only have been combined with the use of impermissible hindsight reconstruction.

Thus, Applicants submit that the present invention would not have been obvious in view of the cited references. Accordingly, withdrawal of the rejection is respectfully requested.

As it is believed that all of the rejections set forth in the Official Action have been fully met, favorable reconsideration and allowance are earnestly solicited.

If, however, for any reason the Examiner does not believe that such action can be taken at this time, it is respectfully requested that he/she telephone applicant's attorney at (908) 654-5000 in order to overcome any additional objections which he might have.

If there are any additional charges in connection with this requested amendment, the Examiner is authorized to charge

Application No.: 10/030,793 Docket No.: ICON 3.3-002

Deposit Account No. 12-1095 therefore.

Dated: March 3, 2005

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Cahiers / Agricultures

Artificial plant chromosomes provide a tool for genetic resource conservation and use

Cahiers d'études et de recherches francophones / Agricultures. Number 9, volume 4, 287-92, Juillet - Août 2000, Ressources génétiques

Résumé Article gratuit

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Summary : Many different genetic resource conservation strategies are available but none of them are universal. They often require complex installations, with high equipment and labour costs. Considering genetic resources at the molecular level, in association with biocomputing and small germplasm collections, now appears to be a reasonable future strategy. Improvement of plant biotechnology techniques has enabled manipulation of large DNA molecules. As a result of the success of yeast artificial chromosomes (YAC), mammalian artificial chromosomes were recently constructed, and should lead to the future construction of plant artificial chromosomes (PAC). Three basic prerequisites are necessary to establish a mitotically stable structure: 1. Origins of replication for chromosome duplication. 2. A centromere to allow the division and migration along the microtubules of duplicated chromosomes into daughter cells. 3. Telomeres at the ends that confer stability. These elements must be of plant origin and mixed with plant chromosomal DNA (from as many plant species as possible) that should in turn be studied and conserved. PAC will be useful to better understand the regulation of gene expression and provide a suitable alternative for genetic resource conservation and use. PAC make it possible to conserve information carried by genes, while regulating their expression, since these structures are established in a similar manner as chromosomes. Data on protein structure and function could also be produced using techniques such as X-ray defraction and magnetic nuclear resonance. If necessary, it will be possible to recreate any allele using all pooled information. Legal and ethic questions will also arise and should be answered.

Keywords :